	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
8	BRS	L8	60309	(sulfhydryl adj reactive) or methanethiosulfonyl or dithiopyridyl or disulfide	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/16 18:31			0
9	BRS	L9	85	7 same 8	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/16 18:32			0
10	BRS	L10	0	6 same 9	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/16 18:33			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	191509	drug	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/16 18:19			0
2	BRS	L2	53	anchoring adj moiety	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/16 18:20			0
3	BRS	L3	2	1 same 2	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/16 18:20			0
4	BRS	L4	82525	anchoring	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/16 18:21			0
5	BRS	L5	218	1 same 4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/16 18:21			0
6	BRS	L6	23	5 same conjugate	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/16 18:25			0
7	BRS	L7	9643	(sodium adj channel) or (calcium adj channel) or (beta-adrenergic adj receptor) or (potassium adj channel) or (membrane adj transporter) or (membrane adj receptor)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/04/16 18:29			0

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?
FILE 'MEDLINE' ENTERED AT 18:34:4[redacted]N 16 APR 2002

FILE 'CAPLUS' ENTERED AT 18:34:42 ON 16 APR 2002
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FILE 'AGRICOLA' ENTERED AT 18:34:42 ON 16 APR 2002

=> s drug
   4 FILES SEARCHED...
L1     8004047 DRUG

=> s (target? molecule) or (anchoring)
L2       35087 (TARGET? MOLECULE) OR (ANCHORING)

=> s l1 (p) l2 (p) conjugate
L3          50 L1 (P) L2 (P) CONJUGATE

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L3
L4           23 DUPLICATE REMOVE L3 (27 DUPLICATES REMOVED)

=> d l4 1-23 ibib abs

L4   ANSWER 1 OF 23  CAPLUS  COPYRIGHT 2002 ACS        DUPLICATE 1
ACCESSION NUMBER:        2001:590412  CAPLUS
DOCUMENT NUMBER:         136:156246
TITLE:                   Metallocene polymers. 51. Polymeric organoiron
                         compounds as prodrugs in cancer research
AUTHOR(S):               Neuse, E. W.
CORPORATE SOURCE:        Department of Chemistry, University of the
                         Witwatersrand, Wits, 2050, S. Afr.
SOURCE:                  Macromolecular Symposia (2001), 172(Polymers in
                         Medicine), 127-138
                         CODEN: MSYMEC; ISSN: 1022-1360
PUBLISHER:               Wiley-VCH Verlag GmbH
DOCUMENT TYPE:           Journal; General Review
LANGUAGE:                English
AB   A review.  Ferrocene, di(.eta.5-cyclopentadienyl)iron(II), has for nearly
     half a century now been a focal point of research activities in the realm
     of organotransition-metal chem. and physics, with ramifications into
     numerous technologies.  More recent years have witnessed the emergence of
     a new research trend, probing the behavior of ferrocene in the biol.
     realms, notably in the transformed, i.e. cancerous, cell system.
     Following initial reports attesting to the pronounced antiproliferative
     properties of certain water-sol. derivs. of ferrocene and its one-electron
     oxidn. product, the ferricenium radical cation, earlier programs were set
     up in the author's lab. with the objective of developing water-sol.
     polymeric   ***conjugates***   in which the bioactive ferrocene unit is
     bioreversibly tied to macromol. carriers in order to enhance its
     therapeutic effectiveness.  In this article, these earlier investigations
     of polymer-ferrocene conjugation are briefly reviewed, and the current,
     considerably broadened synthetic program is introduced.  The carriers are
     predominantly of the highly versatile poly(aspartamide) type, but other
     structures resulting from esteramine polycondensation reactions have been
     included.  Carrier   ***anchoring***   of the ferrocenylation agent of
     choice, 4-ferrocenylbutanoic acid, is brought about both by acylation of
     carrier-attached amino groups, leading to amide links in the spacer, and
     by acylation of polymer-bound hydroxy groups, resulting in ester linking
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of the ferrocene unit. Selected ***conjugates*** are being screened in cell culture tests for antiproliferative activity against HeLa and LNCaP human cancer lines, and preliminary results are highly promising, with IC50 values in the representative range of 2-20 .mu.g Fe/mL. In view of the relatively low level of toxic side effects expected for these organoiron compds., the findings here presented, however limited in scope, offer challenging opportunities for the development of iron-contg., polymer-anchored ***drug*** systems as chemotherapeutic agents in cancer research.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:732747 CAPLUS

TITLE: Fluorescent calcium antagonist: Tools for imaging L-type calcium channel in living cells

AUTHOR(S): Budde, Thomas

CORPORATE SOURCE: Institute of Physiology, Otto-von-Guericke University, Magdeburg, Germany

SOURCE: Ion Channel Localization (2001), 1-15. Editor(s): Lopatin, Anatoli N.; Nichols, Colin G. Humana Press Inc.: Totowa, N. J.
CODEN: 69BXDC

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review on fluorescence techniques used for the direct detection of L-type calcium channels (LTCC) in living cells, based on the development of fluorescent Ca2+ channel blockers, which are ***conjugates*** of Ca2+ antagonist with fluorophores. The location of LTCCs can be detd. with high resoln. in living cells using confocal fluorometric imaging systems. The assocn. and dissocn. kinetics, equil. satn. expts., and ***drug*** interaction studies can be carried out with the aid of spectrofluorometer. The interactions with ***anchoring*** proteins, mechanisms of ***drug*** binding, permeation and gating, fluorescent Ca2+ antagonist will be involved in a new field of studying these channels.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:10616 CAPLUS

DOCUMENT NUMBER: 132:54904

TITLE: Contraceptive compositions containing a synthetic peptide fatty acid conjugate and methods for inhibiting sperm motility using the conjugates

INVENTOR(S): Carr, Daniel W.; Vijayaraghavan, Srinivasan

PATENT ASSIGNEE(S): Oregon Health Sciences University, USA

SOURCE: U.S., 12 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6011013	A	20000104	US 1998-100789	19980618

PRIORITY APPLN. INFO.: US 1997-50314P P 19970620

AB The present invention includes a pharmaceutical compn. having an effective contraceptive amt. of a synthetic peptide that includes an amphipathic .alpha.-helix domain that binds to an RII subunit of protein kinase A, and competitively inhibits the binding of protein kinase A to sperm A kinase anchoring proteins. Particular disclosed synthetic peptides having this activity include s-Ht31: N-Stearate-DLIEEAASRIVDAVIEQVKAAGAY (SEQ ID No. 9), s-Ht31-P: N-Stearate-DLIEEAASRPVDAVPEQVKAAGAY (SEQ ID No. 10), and s-AKAP79: N-Stearate-YETLLIETASSLVKNAIQLSIE (SEQ ID No. 11). The invention also includes methods of inhibiting sperm motility, by exposing them to an effective amt. of the peptide, for example by placing the pharmaceutical compn. (such as a suppository, foam, cream, or gel) in the vagina.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 23 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS I
ACCESSION NUMBER: 2001:253262 BIOSIS
DOCUMENT NUMBER: PREV200100253262
TITLE: Cell-targeting molecule comprising a mutant human carboxypeptidase A.
AUTHOR(S): Smith, Gary Keith (1); Blumenkopf, Todd Andrew; Cory, Michael
CORPORATE SOURCE: (1) Raleigh, NC USA
ASSIGNEE: Glaxo Wellcome Inc.
PATENT INFORMATION: US 6140100 October 31, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 31, 2000) Vol. 1239, No. 5, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB Conjugates of a cell targetting molecule and a mutant human carboxypeptidase A enzyme are provided. Suitable targetting molecules include antibodies, hormones, ligands, cytokines, antigens, oligonucleotides and peptidomimetics. Enzymes comprising a mutant human carboxypeptidase A enzyme are also provided.

L4 ANSWER 5 OF 23 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001061042 MEDLINE
DOCUMENT NUMBER: 20546192 PubMed ID: 11090844
TITLE: Drug-phospholipid conjugates as potential prodrugs: synthesis, characterization, and degradation by pancreatic phospholipase A(2).
AUTHOR: Kurz M; Scriba G K
CORPORATE SOURCE: University of Munster, Department of Pharmaceutical Chemistry, D-48149, Munster, Germany.
SOURCE: CHEMISTRY AND PHYSICS OF LIPIDS, (2000 Oct) 107 (2) 143-57. Journal code: CZW. ISSN: 0009-3084.
PUB. COUNTRY: Ireland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001222
AB The aim of the present study was the synthesis of phospholipids containing a ***drug*** molecule instead of a fatty acid. Valproic acid and ibuprofen served as model compounds. The ***target*** ***molecules*** were synthesized either starting from sn-glycero-3-phosphocholine (1) or using (S)-2-O-benzyl-1-O-tritylglycerol (11) and (R)-2-O-benzyl-1-O-tert-butyldiphenylsilylglycerol (12), respectively, as key intermediates. With respect to the surface properties and the aggregation behavior, the ***drug*** -phospholipid ***conjugates*** resembled natural phosopholipids. Upon incubation with porcine pancreatic phospholipase A(2), only compounds with a fatty acid in the sn-2 position of the glycerol backbone were degraded. Derivatives with either ibuprofen in the sn-2 position or displaying the unnatural S-configuration were resistant to enzymatic in vitro hydrolysis.

L4 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:113561 CAPLUS
DOCUMENT NUMBER: 130:187188
TITLE: Polynucleotide compositions for drug delivery
INVENTOR(S): Kabanov, Alexander V.; Alakov, Valery Y.; Vinogradov, Sergey V.
PATENT ASSIGNEE(S): Supratek Pharma Inc., Can.
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9906035 A1 19990 WO 1998-US16012 19980731
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 6353055 B1 20020305 US 1997-912968 19970801
AU 9886806 A1 19990222 AU 1998-86806 19980731
EP 1003527 A1 20000531 EP 1998-938235 19980731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRIORITY APPLN. INFO.: US 1997-912968 A 19970801
US 1994-342209 A2 19941118
WO 1998-US16012 W 19980731

AB Compns. for stabilizing polynucleic acids and increasing the ability of polynucleic acids to cross cell membranes and act in the interior of a cell. In one aspect, the invention provides a polynucleotide complex between a polynucleotide and certain polyether block copolymers. The polynucleotide complex can further include a polycationic polymer, as well as suitable ***targeting*** ***mols*** . and surfactants. The invention also provides a polynucleotide complex between a polynucleotide and a block copolymer comprising a polyether block and a polycation block. A32P-labeled 17-mer (GGCTCCATTTCTTGCTC) complementary to the 10 transcription initiation site of the HIV-1 tat gene was utilized. A polynucleotide ***conjugate*** of the oligonucleotide was formed with a block copolymer of polyoxyethylene-poly(propyleneimine/butyleneimine). Male C57/B1/6 mice received 50 .mu.L i.v. injections of an anti-HIV ***conjugate*** or free anti-HIV, at 0.18 OD260/.mu.l dissolved in PBS. The plasma levels of the ***drug*** after 30 min were: 75% ***drug*** ***conjugate*** and 20% free ***drug*** .

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 23 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:290913 BIOSIS
DOCUMENT NUMBER: PREV200000290913
TITLE: Spin trapping pharmaceutical compositions and methods for use thereof.
AUTHOR(S): Carney, John M.; Floyd, Robert A.
ASSIGNEE: Oklahoma Medical Research Foundation, Oklahoma City, OK, USA; University of Kentucky Research Foundation
PATENT INFORMATION: US 6002001 December 14, 1999
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 14, 1999) Vol. 1229, No. 2, pp. No pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

AB Spin trapping compositions in general have now been discovered to be effective in treating a variety of disorders, including disorders such as those arising from ischemia, infection, inflammation, exposure to radiation or cytotoxic compounds, not just of the central and peripheral nervous systems but of peripheral organ disease having a wide variety of etiologies. In the preferred embodiment, the compositions for treating tissue damage from ischemia contain PBN, or active derivatives thereof, in a suitable pharmaceutical carrier for intravenous, oral, topical, or nasal/pulmonary administration. Other preferred spin-trapping agents include 5,5-dimethyl pyrroline N-oxide, (DMPO), alpha-(4-pyridyl-1-oxide)-N-tert-butylnitrone, (POBN), and (TEMPO) spin-trapping derivatives thereof. Examples of derivatives of PBN include halogenated derivatives, bifunctional derivatives, ***conjugates*** with ***drugs*** or ***targeting*** ***molecules*** , dimers and cyclodextran polymers of PBN. Many different disorders can be treated using these compounds, including diseases or disorders of the central and peripheral nervous systems, and disorders arising from ischemia, infection, inflammation, oxidation from exposure to radiation or cytotoxic compounds, as well as due to naturally occurring processes such as aging.

L4 ANSWER 8 OF 23 MEDLINE DUPLICATE 3

DOCUMENT NUMBER: 20153045 Pu[redacted]d ID: 10691186
TITLE: Synthesis of aminobenzyltriethylenetetraaminohexaacetic acid: conjugation of the chelator to protein by an alkylamine linkage.
AUTHOR: Bhargava K K; Zhang Z Y; Palestro C J; Acharya S A
CORPORATE SOURCE: Division of Nuclear Medicine, Long Island Jewish Medical Center, New Hyde Park, New York 11040, USA.. bhargava@lij.edu
CONTRACT NUMBER: HL-38655 (NHLBI)
RO1 DK 34251 03 (NIDDK)
SOURCE: JOURNAL OF PROTEIN CHEMISTRY, (1999 Oct) 18 (7) 761-70.
Journal code: AEJ; 8217321. ISSN: 0277-8033.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000323

AB The conjugation of a chelating agent to an antibody as an ***anchoring*** site for a radionuclide is the first step in the successful preparation of a radiolabeled antibody for a diagnostic and therapeutic application. The high affinity of the protein bound chelator towards radionuclide ensures a higher selectivity in the delivery of the radionuclide to the targeted tissue. 4-Aminobenzylderivativetriethlenetetraaminohexaacetic acid (TTHA), a hexadentate chelating agent has been now prepared for conjugation with proteins in view of the higher affinity of TTHA metal ions as compared to DTPA. The latent crosslinking potential of alpha-hydroxy aldehydes has been used to ***conjugate*** the new chelating agent to proteins through an alkylamine linkage. On incubation of amino benzyl TTHA with glycoladehyde at neutral pH and room temperature, the reagent is converted to oxo ethyl amino benzyl TTHA. On addition of albumin to this reaction mixture, the oxo ethylamino benzyl TTHA generates reversible schiff base adducts with the amino groups of albumin. The reduction of the Schiff base adducts of the chelator with the protein by sodium cyanoborohydride stabilizes the schiff base adducts as stable alkylamine linkages. 4-Thiocyanatobenzyl TTHA has also been prepared and conjugated to albumin through a thiocarbamoyl linkage. Both preparations of TTHA conjugated albumin complexed with 99mTc and 111In, with high affinity and no decomposition of the complex was noticed for at least up to 6 hrs after the preparation. The radiolabels complexed with these TTHA -albumin ***conjugates*** could not be 'chased' out by free DTPA. A comparison of the biodistribution of 111In, bound to the TTHA conjugated through an alkylamine and a thiocarbamoyl linkage showed that 111In complexed with alkylamine linked TTHA was retained in blood to a level nearly 17% higher compared to that seen with thicarbamoyl linked TTHA, one hr after the injection into mice. Thus, the alkylamine linkage appears to be more stable under the in vivo conditions. The glycolaldehyde mediated alkylation procedure offers a mild, simple and rapid method for preparation of ***drug*** -protein (antibody) ***conjugates*** .

L4 ANSWER 9 OF 23 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 2001:62689 SCISEARCH
THE GENUINE ARTICLE: 390DR
TITLE: Metallocene polymers 50. Polymer-ferrocene conjugates containing an ester function in the connecting links
AUTHOR: Neuse E W (Reprint); Meirim M G; N''Da D D; Caldwell G
CORPORATE SOURCE: Univ Witwatersrand, Dept Chem, ZA-2050 Wits, South Africa (Reprint)
COUNTRY OF AUTHOR: South Africa
SOURCE: JOURNAL OF INORGANIC AND ORGANOMETALLIC POLYMERS, (DEC 1999) Vol. 9, No. 4, pp. 221-230.
Publisher: KLUWER ACADEMIC/PLENUM PUBL, 233 SPRING ST, NEW YORK, NY 10013 USA.
ISSN: 1053-0495.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 8

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Ferrocene, the parent of the metallocene family of organotransition

compounds, has come to occupy a significant niche in cancer research. Developmental work in the authors' laboratory has been focused on the synthesis of antiproliferative ferrocene ***conjugates*** in which the bioactive ferrocene unit is covalently, yet bioreversibly bound (anchored) to water-soluble carrier polymers designed in accordance with requisite biomedical specifications. The ***anchoring*** link in most of these ***conjugates*** has been an aliphatic spacer containing the biofissionable amide group. In this communication the synthesis of a class of ferrocene ***conjugates*** is reported in which the ferrocene group is carrier-anchored through spacers containing an ester link, of interest here because of potentially different ***drug*** release behavior. The carriers are polyamides equipped with variously spaced hydroxyl side groups, to which the ferrocenylation agent, 4-ferrocenyl-butanoic acid, is connected through esterification. The coupling reactions, mediated by carbodiimide agent and catalyzed by 4-(dimethylamino) pyridine, are carried out in DMF at temperatures not exceeding 65 degreesC, and the water-soluble product polymers are isolated in yields of typically 70-85% by precipitation, aqueous dialysis, and freeze-drying. With the molar feed ratios chosen in these coupling experiments, the incorporation of ferrocene, assessed by H-1 NMR spectroscopy, corresponds to iron contents of roughly 2.5-5.5%, by mass. The ***conjugates*** will be included in a forthcoming bioactivity screening program.

L4 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:180788 CAPLUS
DOCUMENT NUMBER: 128:266240
TITLE: Tumor-homing molecules, conjugates derived therefrom, and methods of using same
INVENTOR(S): Ruoslahti, Erkki; Pasqualini, Renata
PATENT ASSIGNEE(S): Burnham Institute, USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9810795	A2	19980319	WO 1997-US16086	19970910
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9744122	A1	19980402	AU 1997-44122	19970910
EP 927045	A2	19990707	EP 1997-942422	19970910
R: BE, CH, DE, DK, FR, GB, IT, LI, NL, SE				
JP 2001501600	T2	20010206	JP 1998-513856	19970910

PRIORITY APPLN. INFO.: US 1996-710067 A 19960910
WO 1997-US16086 W 19970910

AB The present invention provides tumor-homing mols., which selectively home to a tumor. The invention also provides methods of using a tumor- homing mol. to target an agent, such as a drug, to a selected tumor or to identify the target mol. expressed by the tumor. The invention also provides methods of targeting a tumor contg. angiogenic vasculature by contacting the tumor with a mol. that specifically binds an .alpha.v-contg. integrin. The invention further provides mols. that can selectively home to angiogenic vasculature. In addn., the invention provides a target mol., which is specifically bound by a tumor-homing mol. and is expressed by angiogenic vasculature. The invention also provides antibodies that bind to the target mol. and peptidomimetics that competitively inhibit binding of a ligand to the target mol. Prepn. and antitumor activity of doxorubicin-conjugated peptides are included.

L4 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:58960 CAPLUS
DOCUMENT NUMBER: 128:115236
TITLE: Preparation of conjugates of thrombin inhibitors and endogenes carriers as antithrombotics and blood platelet aggregation inhibitors
INVENTOR(S): Krantz, Alexander; Ezrin, Alan M.; Song, Yonghong
PATENT ASSIGNEE(S): Redcell Canada Inc., Can.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9800171	A2	19980108	WO 1997-IB1093	19970630
WO 9800171	A3	19980604		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5840733	A	19981124	US 1996-674315	19960701
CA 2258516	AA	19980108	CA 1997-2258516	19970630
AU 9740283	A1	19980121	AU 1997-40283	19970630
AU 715746	B2	20000210		
EP 956049	A2	19991117	EP 1997-937767	19970630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000514795	T2	20001107	JP 1998-503954	19970630
US 5942620	A	19990824	US 1998-108534	19980701
KR 2000022371	A	20000425	KR 1998-710802	19981230
US 6087375	A	20000711	US 1999-330744	19990611
US 6277863	B1	20010821	US 2000-599379	20000622

PRIORITY APPLN. INFO.: US 1996-674315 A 19960701
WO 1997-IB1093 W 19970630
US 1998-108534 A1 19980701
US 1999-330744 A1 19990611

OTHER SOURCE(S): MARPAT 128:115236
GI

/ Structure 1 in file .gra /

AB Novel compds. comprising chem. reactive intermediates which can react with available reactive functionalities on blood components to form covalent linkages, where the resulting covalently-bound ***conjugates*** are found to have thrombin inhibition activity are provided. Specifically, the thrombin inhibitor compds. of the present invention are derivs. of the known thrombin inhibitor argatroban represented by formula (I; Y = a linking group of from 2-30 atoms; Z = a chem. reactive group capable of reaction with a reactive functionality of a ***target*** ***mol*** . in an aq. system to form covalent bonds therewith or an activatable precursors to said chem. reactive group; and wherein said compd. possesses thrombin inhibitory activity in vivo when bonded to a long lived blood component), which can be covalently linked to chem. reactive functionalities on various blood components. The conjugated thrombin inhibitors thereby have extended lifetimes in the blood stream, as compared to the unconjugated parent ***drug*** , and are, therefore, capable of maintaining thrombin inhibitory activity for extended periods to time as compared to the unconjugated parent ***drug*** . Also provided herein are methods for inhibiting thrombin activity in vivo comprising administering to the bloodstream of a mammalian host the novel compds. of the present invention. Thus, argatroban monohydrate was condensed with Me 12-aminododecanoate using HBTU coupling agent in DMF to give 28% I.HPF6 [Y-Z = (CH2)11CO2Me] which was hydrolyzed in a mixt. of 1 N aq. NaOH and MeOH and acidified with 1N HCl to pH 3 to give the free acid I.HCl [Y-Z = (CH2)11CO2H] in 85% yield and esterified with N-hydroxysuccinimide by HBTU coupling agent in the presence of (Me2CH)2NEt in DMF to give the N-hydroxysuccinimide active ester I.HCl (Y-Z = Q) in 42% yield. The latter compd. was coupled with human serum albumin (HSA) to give HSA conjugated with argatroban C12-tethered N-hydroxysuccinimide ester which in vitro inhibited thrombin activity from 35-42% at 80 mg/mL and 15-20% at 40 mg/mL compared to control samples.

L4 ANSWER 12 OF 23 MEDLINE DUPLICATE
ACCESSION NUMBER: 1998342124 MEDLINE
DOCUMENT NUMBER: 98342124 PubMed ID: 9675310
TITLE: Comparison of different hydrophobic anchors conjugated to poly(ethylene glycol): effects on the pharmacokinetics of liposomal vincristine.
AUTHOR: Webb M S; Saxon D; Wong F M; Lim H J; Wang Z; Bally M B; Choi L S; Cullis P R; Mayer L D
CORPORATE SOURCE: British Columbia Cancer Agency, 600 West 10th Avenue, Vancouver, B.C. V5Z 4E6, Canada.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1998 Jul 17) 1372 (2) 272-82.
Journal code: A0W; 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 19980917
Entered Medline: 19980904

AB Poly(ethylene glycol) (PEG) conjugated lipids have been used to increase the circulation longevity of liposomal carriers encapsulating therapeutic compounds. PEG is typically conjugated to distearoylphosphatidylethanolamine (DSPE) via a carbamate linkage that results in a net negative charge on the phosphate moiety at physiological pH. It was anticipated that the presence of this negative charge could have deleterious effects on liposome pharmacokinetic characteristics. We describe here the synthesis of a new class of neutrally charged PEG-lipid ***conjugates*** in which the PEG moiety was linked to ceramide (CER). These PEG-CER ***conjugates*** were compared with PEG-DSPE ***conjugates*** for their effects on the pharmacokinetics of liposomal vincristine. PEG-CER (78% palmitic acid, C16) and PEG-DSPE achieved comparable increases in the circulation lifetimes of sphingomyelin/cholesterol (SM/chol) liposomes. However, PEG-DSPE significantly increased the in vitro and in vivo leakage rates of vincristine from SM/chol-based liposomes compared to vincristine leakage observed when PEG-CER was used. The increase in ***drug*** leakage observed in vitro that was due to the presence of PEG-DSPE was likely due to the presence of a negative surface charge. Analysis of the electrophoretic mobilities of these formulations suggested that the negative surface charges were shielded by approx. 80% by the PEG layer extending from the membrane surface. In contrast, formulations containing PEG-CER had no surface charge and no electrophoretic mobility. A comparison of the effects of the ceramide acyl chain length (C8 through C24) on the pharmacokinetics of SM/chol/PEG-CER formulations of vincristine demonstrated that longer acyl chains on the PEG-CER were associated with longer circulation lifetimes of the liposomal carriers and, consequently, higher plasma vincristine concentrations. These data suggest that the short chain PEG-ceramides underwent rapid partitioning from the vesicles after i.v. administration, whereas the longer chain PEG-ceramides had stronger ***anchoring*** properties in the liposome bilayers and partitioned slowly from the administered vesicles. These data demonstrate the utility of ceramide-based steric stabilizing lipids as well as the potential for developing controlled release formulations by manipulating the retention of the PEG-ceramide ***conjugate*** in liposome bilayers.

L4 ANSWER 13 OF 23 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:513392 BIOSIS
DOCUMENT NUMBER: PREV199800513392
TITLE: Alpha-fetoprotein-mediated targeting. A new strategy to overcome multidrug resistance of tumour cells in vitro.
AUTHOR(S): Moskaleva, Elizaveta Yu.; Posypanova, Galina A.; Shmyrev, Igor I.; Rodina, Alla V.; Muizhnek, Ekaterina L.; Severin, Eugene S.; Katukov, Valery Y.; Luzhkov, Yury M.; Severin, Sergei E. (1)
CORPORATE SOURCE: (1) Moscow Res. Inst. Med. Ecol., Sympheropolsky Blvd. 8, Moscow 113149 Russia
SOURCE: Cell Biology International, (Dec., 1997) Vol. 21, No. 12, pp. 793-799.
ISSN: 1065-6995.

DOCUMENT TYPE: Article
LANGUAGE: English
AB The possibility of overcoming the multidrug resistance of human malignant cells by using doxorubicin conjugated to alpha-fetoprotein (AFP) was studied. It was shown that this type of antitumour drugs, penetrating the cell by receptor-mediated endocytosis with AFP as a vehicle, raises the sensitivity of the tumour cells that are resistant due to the expression of the multidrug resistance gene mdr1. The sensitivity of antibiotic-resistant cell lines SKVLB (a human ovarian carcinoma) and MCF-7 AdrR (a human breast carcinoma) increased by 10- and 4-fold, respectively, when AFP-conjugated doxorubicin was used. The rationale of using human AFP-antitumour drug conjugates for the development of new chemotherapeutic approaches to cancer treatment is discussed.

L4 ANSWER 14 OF 23 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 96230084 MEDLINE
DOCUMENT NUMBER: 96230084 PubMed ID: 8666314
TITLE: Adenine arabinoside monophosphate coupled to lactosaminated human albumin administered for 4 weeks in patients with chronic type B hepatitis decreased viremia without producing significant side effects.
AUTHOR: Torrani Cerenzia M; Fiume L; De Bernardi Venon W; Lavezzo B; Brunetto M R; Ponzetto A; Di Stefano G; Busi C; Mattioli A; Gervasi G B; Bonino F; Verme G
CORPORATE SOURCE: Ospedale Molinette, Torino, Italy.
SOURCE: HEPATOLOGY, (1996 Apr) 23 (4) 657-61.
Journal code: GBZ; 8302946. ISSN: 0270-9139.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960819
Last Updated on STN: 19960819
Entered Medline: 19960802
AB A ***conjugate*** of adenine arabinoside monophosphate (ara-AMP) with the liver- ***targeting*** ***molecule*** lactosaminated human serum albumin (L-HSA) was administered by intravenous infusion for 28 days to eight patients with chronic type B hepatitis. The daily dose varied among the patients, ranging from 34 mg/kg to 53 mg/kg (equal to 1.5 and 2.3 mg/kg ara-AMP, respectively). Pharmacokinetic analysis indicated that, at every dose tested, the ***conjugate*** was disposed of without accumulation. Viral DNA serum levels fell markedly during treatment; values rose again when treatment was ceased. The L-HSA-ara-AMP ***conjugate*** did not cause either the neurotoxic side effects of free ara-AMP or other adverse clinical reactions. It produced a significant increase both in serum alkaline phosphatase activity and platelet number, and a small but significant decrease in erythrocyte number. These laboratory parameters returned to normal levels within 2 months after treatment. The ***conjugate*** induced the production of small amounts of antibodies (approximately 20 pmol of ***conjugate*** bound by 1 mL of serum) in one patient only. In conclusion, the present results indicate that the L-HSA-ara-AMP ***conjugate*** can exert the antiviral activity of ara-AMP in chronic type B hepatitis patients without producing the neurotoxic side effects which hamper a 4-week period of treatment with the free ***drug*** .

L4 ANSWER 15 OF 23 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 95402627 MEDLINE
DOCUMENT NUMBER: 95402627 PubMed ID: 7672506
TITLE: Flavoprotein structure and mechanism. 5. Trypanothione reductase and lipoamide dehydrogenase as targets for a structure-based drug design.
AUTHOR: Krauth-Siegel R L; Schoneck R
CORPORATE SOURCE: Institut fur Biochemie II, Universitat Heidelberg, Germany.
SOURCE: FASEB JOURNAL, (1995 Sep) 9 (12) 1138-46. Ref: 49
Journal code: FAS; 8804484. ISSN: 0892-6638.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English

DOCUMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 19951026
Last Updated on STN: 19951026
Entered Medline: 19951019

AB Trypanothione reductase (TR) is a flavoenzyme that has been found only in parasitic protozoa of the order Kinetoplastida. The enzyme catalyzes the NADPH-dependent reduction of glutathionylspermidine ***conjugates*** and is a key enzyme of the parasite's thiol metabolism. Consequently, TR is an attractive ***target*** ***molecule*** for a structure-based ***drug*** development against Chagas' disease, African sleeping sickness, and other diseases caused by trypanosomes and leishmanias. The three-dimensional structures of TR and of three enzyme substrate complexes have been solved. Several classes of compounds are discussed as guide structures for the design of specific inhibitors. Among them are tricyclic compounds such as acridines and phenothiazines, which competitively inhibit TR but not the related host enzyme glutathione reductase, as well as oxidase activity-inducing quinones and nitrofurans. Lipoamide dehydrogenase (LipDH) is another flavoprotein discussed as a ***target*** ***molecule*** for an antitrypanosomal therapy. In Trypanosoma cruzi, an organism that is highly susceptible to oxidative stress, LipDH participates in the redox cycling of nifurtimox, one of the most effective anti-Chagas agents. In conclusion, the structurally related enzymes TR and LipDH exhibit an unusually high one-electron-reducing capacity. Consequently, turncoat inhibitors and other compounds inducing an oxidase activity in both enzymes are promising ***drug*** candidates against Chagas' disease.

L4 ANSWER 16 OF 23 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 7
ACCESSION NUMBER: 95192171 EMBASE
DOCUMENT NUMBER: 1995192171
TITLE: Functional models of the antitumor antibiotic bleomycin.
AUTHOR: Huang L.; Quada Jr. J.C.; Lown J.W.
CORPORATE SOURCE: Department of Chemistry, University of Alberta,Edmonton, Alta. T6G 2G2, Canada
SOURCE: Current Medicinal Chemistry, (1995) 2/1 (543-560).
ISSN: 0929-8673 CODEN: CMCHE7
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The naturally occurring glycopeptide bleomycin exhibits both antitumor and antibiotic properties. It has an established place in the clinical treatment of certain human malignancies including squamous cell carcinoma and testicular tumors. Structurally it comprises four distinct domains: i) an ***anchoring*** group containing a bithiazole moiety that binds to double helical DNA; ii) a chiral peptidic spacer that positions the individual portions of the molecule on the receptor; iii) a sugar moiety bearing a carbamoyl group; and iv) an active moiety bearing ligands capable of coordinating a metal ion, such as iron and which is involved in the redox chemistry ultimately responsible for site specific DNA damage. The observation of serious side effects, principally pulmonary toxicity, has limited the clinical applications of bleomycin and provides the motivation to develop less toxic and more selective versions of the ***drug*** . Once the mechanism of action of bleomycin via oxygen mediated and site specific DNA cleavage was elucidated the possibility arose of designing functional models. This article will review progress from the earliest metal-complexing models to the most recent ***conjugates*** that fully mimic the action of the natural product and, moreover, are capable of being directed to alternative target sequences.

L4 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
ACCESSION NUMBER: 1995:685078 CAPLUS
DOCUMENT NUMBER: 123:122893
TITLE: Polymers in drug delivery: immunotargeting of carrier-supported cis-platinum complexes
AUTHOR(S): Schechter, Bilha; Arnon, Ruth; Wilchek, Meir
CORPORATE SOURCE: Dep. Chem. Immunol., Weizmann Inst. Sci., Rehovot, 76100, Israel

React. Polym. (1995), 25(2/3), 167-75
CODEN: RPOLEN; ISSN: 0923-1137
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cisplatin (CDDP), a most powerful anticancer agent, was complexed to a polycarboxylic carrier carboxymethyl dextran to form a platinum(II) multicomplex. Complexing occurred by displacement of the chlorine atoms of the platinum coordination complex by hydrogen of polymer side-chains to form mono- or bifunctional ***anchoring*** to adjacent carboxyls on the carrier. The carrier-complexed ***drug*** interacted with DNA and was pharmacol. active against tumor cells. The ***drug*** -carrier complex was immunotargeted to human epidermoid carcinoma (KB) tumors, using the monoclonal antibody (mAb) 108 directed against the epidermal growth factor receptor that is overexpressed on KB cells. Biotinyl-monoclonal antibody was bound to a platinum(II)-carboxymethyl dextran-avidin ***conjugate*** and the immune complex was administered into established s.c. KB tumors to evaluate. its effects upon intratumor treatment. The results showed that the immune complex was specifically effective in inhibiting tumor growth. The antibody in the complex must be tumor-specific to anchor the ***drug*** -carrier multicomplex to the tumor site since an unbiotinylated antibody, or replacing the anti-KB antibody by a biotinylated antibody of a different specificity, resulted in reduced or abolished inhibitory effects.

L4 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 9
ACCESSION NUMBER: 1994:307200 CAPLUS
DOCUMENT NUMBER: 120:307200
TITLE: Water-soluble polyamides as potential drug carriers. VII. Synthesis of polymers containing intrachain- or extra-chain-type amine ligands by interfacial polymerization
AUTHOR(S): Chiba, Urvashi; Neuse, Eberhard W.; Swarts, Jannie C.; Lamprecht, Gert J.
CORPORATE SOURCE: Dep. Chem., Univ. Witwatersrand, Wits, 2050, S. Afr.
SOURCE: Angew. Makromol. Chem. (1994), 214, 137-52
CODEN: ANMCBO; ISSN: 0003-3146
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aliph. polyamides comprising poly(ethylene oxide) chain segments of various lengths, designed for use as ***drug*** carriers, were prepd. by interfacial polymn. of succinyl chloride with the 2 Jeffamine types ED-900 and ED-2001, formally described by the supplier as O,O'-bis(2-aminopropyl)poly(ethylene glycol) 800 and O,O'-bis(2-aminopropyl)poly(ethylene glycol) 1900. Copolyamides comprising both short-chain diamine and Jeffamine segments were similarly prepd., as were polyamides made up of cystine and diamine segments. The polymns. were performed in a 2-phase CH2Cl2 system at temps. near or below 0.degree.. The product polymers, crudely fractionated by staged aq.-phase dialysis at an ultimate mol.-mass cut-off of 25,000, are collected after freeze-drying as water-sol. resins or solids and are characterized microanalytically and by 1H-NMR spectroscopy. Inherent viscosities are in the range of 10-20 mL g-1. The ***drug*** -binding potential of a representative target polymer is probed by the covalent ***anchoring*** of a ferrocene compd. used as a ***drug*** model, giving a water-sol. polymer-ferrocene ***conjugate*** .

L4 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:116773 CAPLUS
DOCUMENT NUMBER: 118:116773
TITLE: spin trapping agents for the treatment of diseases associated with oxidation of lipids and proteins
INVENTOR(S): Carney, John M.; Floyd, Robert A.
PATENT ASSIGNEE(S): Oklahoma Medical Research Foundation, USA; University of Kentucky Research Foundation
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9222290	A1	19921[redacted]	WO 1992-US5194	199206[redacted]	
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US					
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG					
AU 9222614	A1	19930112	AU 1992-22614	19920618	
AU 672364	B2	19961003			
EP 590072	A1	19940406	EP 1992-914539	19920618	
EP 590072	B1	20011205			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE					
AT 209908	E	20011215	AT 1992-914539	19920618	
CA 2111836	AA	19921223	CA 1992-2111836	19921223	
US 5622994	A	19970422	US 1994-212800	19940315	
US 6002001	A	19991214	US 1997-969344	19971128	

PRIORITY APPLN. INFO.:	US 1991-716952	A2	19910618
	US 1989-422651	A2	19891017
	US 1990-589177	B2	19900927
	WO 1992-US5194	A	19920618
	US 1993-52870	B1	19930426
	US 1994-212800	A2	19940315
	US 1994-167900	B1	19940729

OTHER SOURCE(S): MARPAT 118:116773

AB In the preferred embodiment of the invention, compns. for treating tissue damage from ischemia contain .alpha.-Ph tert-Bu nitrone (I), or active derivs. thereof, in a suitable pharmaceutical carrier. Other preferred spin-trapping agents include 5,5-dimethylpyrroline N-oxide, .alpha.-(4-pyridyl-1-oxide)-N-tert-butylnitrone, TEMPO, and derivs. thereof. The I derivs. include halo derivs., bifunctional derivs., ***conjugates*** with ***drugs*** or ***targeting*** ***mols*** ., dimers, and cyclodextran polymers of I. Many different disorders can be treated using these compds., including diseases or disorders of the central and peripheral nervous systems and disorders arising from ischemia, infection, inflammation, oxidn. from exposure to radiation or cytotoxic compds., as well as due to naturally occurring processes (e.g. aging). I inhibited oxidn. of LDL in plasma in vitro.

L4 ANSWER 20 OF 23 SCISEARCH COPYRIGHT 2002 ISI (R)

ACCESSION NUMBER:	91:490070 SCISEARCH
THE GENUINE ARTICLE:	GC601
TITLE:	AMINE-FUNCTIONALIZED, WATER-SOLUBLE POLYAMIDES AS DRUG CARRIERS
AUTHOR:	NEUSE E W (Reprint); PERLWITZ A G
CORPORATE SOURCE:	UNIV WITWATERSRAND, DEPT CHEM, WITWATERSRAND 2050, SOUTH AFRICA (Reprint)
COUNTRY OF AUTHOR:	SOUTH AFRICA
SOURCE:	ACS SYMPOSIUM SERIES, (1991) Vol. 467, pp. 394-404.
DOCUMENT TYPE:	Article; Journal
LANGUAGE:	ENGLISH
REFERENCE COUNT:	26

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Solubility in aqueous media is a prerequisite for the efficacious ***drug*** carrier action of polymeric carrier molecules designed for the reversible binding of certain pharmacologically active agents requiring intravenous or intracavitary administration in clinical use. The macromolecular carriers discussed in this communication are aliphatic polyamides possessing intrachain-type or side chain-attached, primary or secondary amine functions capable of ***drug*** binding. The polymers are perfectly soluble in water, which permits a rough fractionation by dialysis. The products retained in membrane tubing with 12000 - 14000 molecular-mass cut-off have inherent viscosities of 5-20 mL g-1. Several side-chain modification and model ***drug*** ***anchoring*** reactions are described, all leading to water-soluble product polymers. Notable among these are ***conjugates*** with organoiron (ferrocene) or platinum coordination complexes as examples of the pharmacologically important class of metal-containing polymeric ***drugs*** .

L4 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1991:400778 CAPLUS
DOCUMENT NUMBER:	115:778
TITLE:	Covalently-linked complexes and methods for enhanced cytotoxicity and imaging

INVENTOR(S): Anderson, David C.; Morgan, A. Charles; Abrams, Paul G.; Nich[redacted], Everett J.; Fritzberg, Alan [redacted]
PATENT ASSIGNEE(S): NeoRx Corp., USA
SOURCE: Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 359347	A2	19900321	EP 1989-250014	19890814
EP 359347	A3	19900418		
EP 359347	B1	19921223		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5135736	A	19920804	US 1988-232337	19880815
US 5169933	A	19921208	US 1989-390241	19890807
CA 1334513	A1	19950221	CA 1989-608198	19890811
JP 02124833	A2	19900514	JP 1989-209992	19890814
AT 83669	E	19930115	AT 1989-250014	19890814

PRIORITY APPLN. INFO.: US 1988-232337 19880815
EP 1989-250014 19890814

AB Covalently-linked complexes (CLCs) for targeting a defined population of cells comprise a targeting protein (e.g. antibody, hormone, enzyme, etc.), a cytotoxic agent (e.g. radionuclide, toxin, ***drug*** , etc.) an enhancing moiety capable of enhancing CLC-target cell interaction (e.g. a translocating/internalizing moiety, an ***anchoring*** peptide, membrane-sol. hydrophobic mol., etc.). The CLCs are used to enhance in vivo cytotoxicity and imaging (no data). Translocating peptide, Cys-Gly-Glu-Ala-Ala-Leu-Ala(Glu-Ala-Leu-Ala)4-Glu-Ala-Leu-Glu-Ala-Leu-Ala-Ala-NH2, is conjugated via succinimidyl 4(N-maleimidemethyl)cyclohexane-1-carboxylate (SMCC) to reduced toxin A chain. The ***conjugate*** is reacted with iminothiolane to generate further thiol groups which are then bonded to reduced antibody to prep. translocating peptide-ricin A chain-antibody CLC.

L4 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 10
ACCESSION NUMBER: 1991:82486 CAPLUS
DOCUMENT NUMBER: 114:82486
TITLE: Water-soluble polyamides as potential drug carriers. II. Amine-functionalized poly(.alpha.,.beta.-D,L-aspartamide) derivatives
AUTHOR(S): Neuse, Eberhard W.; Perlwitz, Axel; Schmitt, Siegfried
CORPORATE SOURCE: Dep. Chem., Univ. Witwatersrand, Wits, 2050, S. Afr.
SOURCE: Angew. Makromol. Chem. (1990), 181, 153-70
CODEN: ANMCBO; ISSN: 0003-3146
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several derivs. of poly(.alpha.,.beta.-DL-aspartic acid) (I) comprising amine functions as side chain components are synthesized for use as macromol. ***drug*** carriers. The structures of the target polymers are designed so as to provide complete soly. in water, a prerequisite for smooth i.v. administration, and the strategy of derivatization reflects the requirement for the performance of all reaction steps in a partially or entirely aq. phase. I, a known synthetic polyamide obtained from poly(succinimide) (II) and composed of both .alpha.- and .beta.-peptide units in the chain, is coupled with ethylenediamine, diethylenetriamine, N-(2-hydroxyethyl)ethylenediamine, and hydrazine in the presence of water-sol. carbodiimides. This gives poly(aspartamides) possessing primary amino side groups. More efficaciously, circumventing the intermediacy of the polyacid I, the polymers are obtained through nucleophilic opening of the imide rings in II by the same amine reactants. The anal. and spectroscopically characterized, water-sol. target polymers have inherent viscosities ranging from 5 to 20 mL g-1 and possess the structural prerequisites for side-chain ***drug*** ***anchoring*** involving the spacer-bound amino groups. The susceptibility of these functional groups to substitution as a measure of their ***drug*** binding capabilities is demonstrated by their conversion to N-acryloylated derivs. and by condensation of 5-formylsalicylic acid with the bidentate ethylenediamine side group-contg. polymer to give the ***conjugate*** contg. the bioactive salicyloyl group as a side chain component.

L4 ANSWER 23 OF 23 MEDLINE DUPLICATE
ACCESSION NUMBER: 83155207 MEDLINE
DOCUMENT NUMBER: 83155207 PubMed ID: 6925984
TITLE: Inhibition of a mouse hepatoma by the alkylating agent Trenimon linked to immunoglobulins.
AUTHOR: Ghose T; Guclu A; Raman R R; Blair A H
SOURCE: CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1982) 13 (3) 185-9. Journal code: CN3; 8605732. ISSN: 0340-7004.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198305
ENTRY DATE: Entered STN: 19900318
Last Updated on STN: 19900318
Entered Medline: 19830527
AB Trenimon was conjugated in active alkylating form to rabbit anti-mouse H6 hepatoma globulin (AHG) with retention of antibody activity. H6 hepatoma-inoculated mice were given various combinations of ***conjugates*** , free Trenimon, and unconjugated immunoglobulins in daily injections for 5 days. Linkage of Trenimon to immunoglobulins reduced systemic toxicity of the ***drug*** , with comparative retention of its antitumor activity. The antitumor action of Trenimon was potentiated by AHG irrespective of whether the ***drug*** was directly linked to AHG or free AHG was administered along with Trenimon linked to normal rabbit globulin (NRG). In vitro, Trenimon bound to AHG was less inhibitory to hepatoma cells than free Trenimon, but more inhibitory than Trenimon-NRG ***conjugates*** . There was no significant endocytosis of ***conjugates*** by the hepatoma cells. This suggests that unlike free Trenimon, the ***target*** ***molecules*** of Trenimon-immunoglobulin ***conjugates*** are not intracellular DNA but are located on the surface of the hepatoma cells.

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(FILE 'HOME' ENTERED AT 18:34:14 ON 16 APR 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 18:34:42 ON 16 APR 2002
L1 8004047 S DRUG
L2 35087 S (TARGET? MOLECULE) OR (ANCHORING)
L3 50 S L1 (P) L2 (P) CONJUGATE
L4 23 DUPLICATE REMOVE L3 (27 DUPLICATES REMOVED)

=> s (sodium channel) or (calcium channel) or (beta-adrenergic receptor) or (potassium channel) or
4 FILES SEARCHED...
L5 405429 (SODIUM CHANNEL) OR (CALCIUM CHANNEL) OR (BETA-ADRENERGIC RECEPT OR) OR (POTASSIUM CHANNEL) OR (MEMBRANE TRANSPORTER) OR (MEMBRAN E RECEPTOR)

=> s methnethiosulfonyl or dithiopyridyl or (reactive disulfide)
L6 280 METHNETHIOSULFONYL OR DITHIOPYRIDYL OR (REACTIVE DISULFIDE)

=> s l5 (p) l6
L7 5 L5 (P) L6

=> duplicate remove l7
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L7
L8 1 DUPLICATE REMOVE L7 (4 DUPLICATES REMOVED)

=> d l8 1 ibib abs

L8 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000405733 MEDLINE
DOCUMENT NUMBER: 20295167 PubMed ID: 10833532
TITLE: Skeletal muscle ryanodine receptor channels are activated by the fungal metabolite, gliotoxin.
AUTHOR: Green D; Pace S M; Hurne A M; Waring P; Hart J D; Dulhunty

A F
CORPORATE SOURCE: John Curtin S ol of Medical Research, PO Box 4,
Canberra, ACT 2601, Australia.
SOURCE: JOURNAL OF MEMBRANE BIOLOGY, (2000 Jun 1) 175 (3) 223-33.
Journal code: J4E; 0211301. ISSN: 0022-2631.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000901
Last Updated on STN: 20000901
Entered Medline: 20000818

AB Interactions between the ***reactive*** ***disulfide*** fungal metabolite, gliotoxin (GTX), and rabbit skeletal ryanodine receptor (RyR) calcium release channels have been examined. RyRs in terminal cisternae vesicles formed a covalent complex with 100 &mgr;m (35)S-GTX, which was reversed by 1 mm dithiothreitol (DTT) or 1 mm glutathione. GTX (80-240 &mgr;m), added to either cytoplasmic (cis) or luminal (trans) solutions, increased the rate of Ca(2+) release from SR vesicles and the frequency of opening of single RyR channels in lipid bilayers. Channel activation was reversed upon addition of 2 mm DTT to the cis solution, showing that the activation was due to an oxidation reaction (2 mm DTT added to the cis solution in the absence of GTX did not affect RyR activity). Furthermore, RyRs were not activated by trans GTX if the cis chamber contained DTT, suggesting that GTX oxidized a site in or near the membrane. In contrast to cis DTT, 2 mm DTT in the trans solution increased RyR activity when added either alone or with 200 &mgr;m trans GTX. The results suggest that (i) GTX increases RyR channel activity by oxidizing cysteine residues that are close to the membrane and located on RyR, or associated proteins, and (ii) a disulfide bridge or nitrosothiol, accessible only from the luminal solution, normally suppresses RyR channel activity. Some of the actions of GTX in altering Ca(2+) homeostatsis might depend on its modification of RyR ***calcium*** ***channels*** .

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(FILE 'HOME' ENTERED AT 18:34:14 ON 16 APR 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 18:34:42 ON 16 APR 2002
L1 8004047 S DRUG
L2 35087 S (TARGET? MOLECULE) OR (ANCHORING)
L3 50 S L1 (P) L2 (P) CONJUGATE
L4 23 DUPLICATE REMOVE L3 (27 DUPLICATES REMOVED)
L5 405429 S (SODIUM CHANNEL) OR (CALCIUM CHANNEL) OR (BETA-ADRENERGIC REC
L6 280 S METHNETHIOSULFONYL OR DITHIOPYRIDYL OR (REACTIVE DISULFIDE)
L7 5 S L5 (P) L6
L8 1 DUPLICATE REMOVE L7 (4 DUPLICATES REMOVED)

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	87.88	88.09

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-6.82	-6.82

STN INTERNATIONAL LOGOFF AT 18:41:12 ON 16 APR 2002